REMARKS

I. Status of the Application

This paper responds to a final Office action mailed December 9, 2005, which rejected claims 1-14, 16 and 17. The application was originally filed with claims 1-15. Following a first Office action, mailed September 13, 2004, Applicant amended claims 1-3, 5-10, and 13-15. In response to a final Office action, mailed February 28, 2005, Applicant filed an RCE which included an after final amendment that modified claim 14, canceled claim 15 without prejudice or disclaimer, and added claim 16. Following an Office action mailed June 21, 2005, Applicant amended claims 1, 2, 6, 7, 9, 10-12, 14 and 16, and added new claim 17. The present paper amends claim 16, cancels claim 17 without prejudice or disclaimer, and adds new claim 18. Therefore, claims 1-14, 16 and 18 are currently under consideration in the present application. Applicant respectfully requests reconsideration of the pending claims in view of the above amendment and the following remarks. By action taken here, Applicant does not intend to surrender any range of equivalents beyond that needed to patentably distinguish the claimed invention as a whole over the prior art. Applicant expressly reserves all such equivalents that may fall in the range between Applicant's literal claim recitations and combinations taught or suggested by the prior art.

II. Amendment of Claim 16 and Addition of New Claim 18

Applicant has amended claim 16 so that it refers to compositions recited in claims 1, 14 and 18. New claim 18 includes the limitations of claim 1, but also recites a specific gamma-aminobutyric acid analog (gabapentin) and two specific polyhydric alcohols (xylitol and glycerol). Support for these limitations can be found throughout the specification, including at page 5, lines 19-21 and page 9, lines 29-31.

III. Rejection of Claim 17 Under 35 U.S.C. § 112 ¶ 1

The final Office action rejected claim 17 under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. Although Applicant has canceled claim 17 which obviates the rejection, Applicant respectfully

submits that claim 17 is fully supported in the application as filed. See specification at page 5, lines 19-21; page 9, lines 29-31; page 12, Table 1; and original claim 14.

IV. Rejection of claims 1-14, 16 and 17 Under 35 U.S.C. § 103

The final Office action rejected claims 1-14, 16 and 17 under 35 U.S.C. § 103 as being unpatentable over WO 99/58573. According to a prior Office action, which has been incorporated into the final Office action, "WO 99/59573 (page 50, lines 7-21, pages 58-61, Examples 2 and 3) discloses a liquid composition of a GABA analog comprising a polyhydric alcohol containing 2-6 carbon atoms. It discloses the use of a sweetening agent and a flavoring agent on page 50. The examples further disclose formation of the lactam degradation product is limited by the addition of the polyhydric alcohol." Applicant respectfully submits that claims 1-14, 16 and 18 are patentable over WO 99/59573 and all other references cited in the case.

Applicant submits that WO 99/58573 does not render the claims obvious. As noted in the application, Applicant has discovered that a GABA analog can be formulated in a stable liquid pharmaceutical composition having low levels of a GABA analog lactam when the pH of the composition is about 5.5 to about 7.0 and when the composition includes one or more polyhydric alcohols. See Specification, page 4, lines 4-7, and page 9, lines 7-9. Nothing in WO 99/59573 teaches or suggests that this pH range and the addition of one or more polyhydric alcohols in the claimed amounts would result in a stable liquid pharmaceutical composition containing a GABA analog.

As discussed in the previous response, WO 99/59573 teaches away from the use of a polyhydric alcohol in pharmaceutical compositions containing a GABA analog. For instance, Example 2 in WO 99/59573 shows that the addition of a polyhydric alcohol (xylitol, sample "e") to an aqueous gabapentin solution increases lactam formation (compare sample "d" and sample "e" in Table 4). The addition of glycine (sample "f") to an aqueous solution of gabapentin and xylitol appears to decrease lactam formation (compare sample "f" with samples "d" and "e" in Table 4). Thus, WO 99/59573 states that Table 4 "shows that gabapentin in its aqueous solution could be similarly prevented

from the degradation with lapse of time (the lactam formation) by the addition of glycine, even in the presence of xylitol," i.e., despite the presence of xylitol (emphasis added).

The final Office action contends that WO 99/59573 does not teach away from the claimed invention because "the 'comprising' language of the claims would allow for both xylitol and glycine ... ." Applicant agrees that the claims would permit xylitol and glycine in the composition. However, the claim scope does not affect what WO 99/59573 teaches—that xylitol increases lactam formation and glycine prevents lactam formation even in the presence of xylitol. Applicant respectfully submits that this teaching is contrary to what is claimed. Indeed, the claims of the present application require that the pharmaceutical compositions include a polyhydric alcohol (e.g., xylitol), which WO 99/59573 suggests would destabilize the formulations. Furthermore, the claims do not require that the pharmaceutical compositions include glycine, which WO 99/59573 teaches would be needed to ensure stability of compositions containing xylitol.

Applicant further submits that the claimed pH range and the use of one or more polyhydric alcohols in the claimed amounts result in pharmaceutical compositions having surprising and unexpected chemical stability. To support this conclusion, Applicant has attached to this amendment a declaration under 37 CFR § 1.132. As described in the declaration, a number of samples were prepared that contain water, gabapentin, and a polyhydric alcohol (xylitol or glycerol) to examine the influence of pH and the presence of a polyhydric alcohol on lactam formation. The compositions of the samples are shown in Table 1 of the declaration. All of the samples contained 5% w/v gabapentin (5 g per 100 mL of the composition). Samples of formulation A contained no polyhydric alcohol. Samples of formulations B, C, D, and E contained 15%, 25%, 40%, and 75% w/v xylitol, respectively. Samples of formulations F, G, H, and I contained 15%, 25%, 40%, and 75% w/v glycerol, respectively. The initial pH of the samples was adjusted, when necessary, by adding an acid or base, and ranged from pH 3 to pH 9.

According to the declaration, samples of liquid formulations A-I in Table 1 were subjected to stability testing at elevated temperature in a manner similar to Example 2 of WO 99/59573. Using a validated HPLC assay method, the amount of lactam in each

sample was measured following 1, 2 or 3 weeks storage at 45°C. The amount of lactam was calculated as the percentage of lactam (mg) found in the sample relative to the amount of gabapentin (mg) in the original sample preparation.

Tables 2-4 of the declaration list the amount of lactam present in the samples after storage at 45°C for 1, 2 or 3 weeks, respectively. The data indicate that aqueous compositions containing gabapentin exhibit improved stability when formulated at a pH of about 5.5 to about 7.0. See Table 2, formulations A, B and D. The data also indicate that aqueous gabapentin formulations containing a polyhydric alcohol generally exhibit improved stability over formulations that do not. Compare, e.g., formulations B-D, F and G in Table 2 with formulation A. Generally, the most improvement in stability occurs for formulations containing 15% w/v of polyhydric alcohol, but in some cases higher concentrations of polyhydric alcohol may have the same impact on stability as lower concentrations. Compare, e.g., formulations A, B and D in Table 2 having pH of 7.0. The data also suggest that sample e in Example 2 of WO 99/59573, which contained 5% w/v gabapentin and 15% w/v xylitol, was formulated at a pH outside the range of pH 6.0 to 7.3.

Based on the data in the declaration, Applicant submits that the claimed pH range and the use of one or more polyhydric alcohols in the claimed amounts result in pharmaceutical compositions having surprising and unexpected chemical stability. Applicant submits that claims 1-14, 17 and 18 are therefore patentable over WO 99/59573 and all references cited in the case and respectfully requests withdrawal of the rejection.

V. Conclusion

In view of the foregoing, Applicant respectfully submits that all pending claims are patentable over the prior art of record. If the Examiner has any questions, Applicant requests that the Examiner telephone the undersigned.

Applicant submits that all fees due in connection with the filing of this paper have been identified in an accompanying fee transmittal. However, if any such fees have not been identified in the accompanying fee transmittal, please charge deposit account number 23-0455.

Respectfully submitted,

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Matthew J. Russo, Reg. No. 41,282
Warner-Lambert Company LLC
2800 Plymouth Road
Ann Arbor, MI 48105
Tel: (734) 622-1747
Fax:(734) 622-2928
Customer No. 28880